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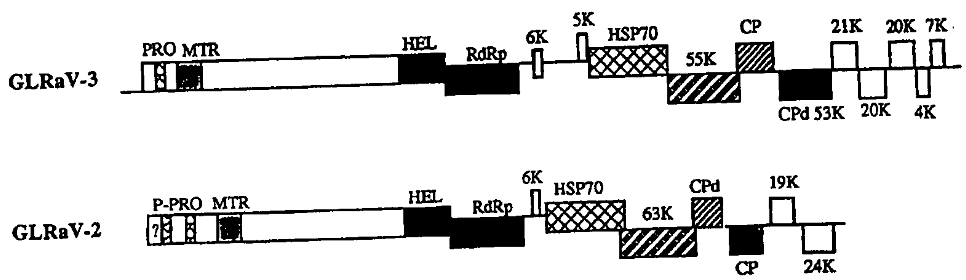

(57) Abstract

The present invention relates to an isolated GLRaV-3 protein or polypeptide selected from a group of a polyprotein, a proteinase, a methyltransferase, a helicase, and an RNA-dependant RNA polymerase. The encoding DNA molecule either alone in isolated form or in an expression system, a host cell, or a transgenic grape plant is also disclosed. Another aspect of the present invention relates to a method of imparting grapevine leafroll resistance to grape plants by transforming them with the DNA molecule of the present invention.

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GRAPEVINE LEAFROLL VIRUS PROTEINS AND THEIR USES

Cross-reference to Related Applications

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Background of the Invention

The present invention relates to grapevine leafroll virus genomic DNA, RNA, proteins encoded thereby, and their uses.

The world's most widely grown fruit crop, the grape (*Vitis sp.*), is cultivated on all continents except Antarctica. Many plant pathogens, such as fungi, bacteria, phytoplasmas, viruses, and nematodes can infect grapes, and the resultant diseases can cause substantial losses in production thereof (Pearson et al., Compendium of Grape Diseases, American Phytopathological Society Press (1988)). Among these, viral diseases constitute a major hindrance to profitability.

About 34 viruses have been isolated and characterized from grapevines. The major virus diseases are grouped into: (1) nepoviruses, (2) the leafroll complex (GVLR), and (3) the rugose wood complex (Martelli, ed., Graft Transmissible Diseases of Grapevines, Handbook for Detection and Diagnosis, FAO, UN, Rome, Italy (1993)). The grapevine leafroll complex (GVLR) is most widely distributed throughout the world. The virus was first identified in 1946 by Harmon et al. (Proc. Am. Soc. Hort. Sci. 74:190-194 (1946)) and later confirmed by Goheen et al. (Phytopathology, 48:51-54 (1958)). Leafroll is a serious virus disease and occurs wherever grapes are grown. Although the disease is not lethal, it causes yield losses and reduction in sugar content. For example, the amount of sugar in individual berries

of infected vines is only about 1/2 to 2/3 that of berries from noninfected vines (Goheen, supra).

Several virus particle types have been isolated from leafroll diseased vines. These include potyvirus-like (Tanne et al., Phytopathology, 67:442-447 (1977)), isometric virus-like (Castellano et al., Vitis, 22:23-39 (1983)) and closterovirus-like (Namba, Ann. Phytopathol. Soc. Japan, 45:497-502 (1979)) particles. In recent years, however, long flexuous closteroviruses ranging from 1,400 to 2,200 nm have been most consistently associated with leafroll disease as shown, for example, in Castellano (1983), Faoro et al., Riv. Patol. Veg., Ser IV, 17:183-189 (1981), Hu et al., J. Phytopathol., 128:1-14 (1990), Milne et al., Phytopathol. Z., 110:360-368 (1984), and Zimmermann et al., J. Phytopathol., 130:205-218 (1990). These closteroviruses are referred to as grapevine leafroll associated viruses ("GLRaV"). At least six serologically distinct types of GLRaV's (GLRaV-1 to -6) have been detected from leafroll diseased vines (Boscia et al, Vitis, 34:171-175 (1995)).

Grapevine leafroll is transmitted primarily by contaminated scions and rootstocks. Under field conditions, however, several species of mealybugs have been shown to be the vector of leafroll (Engelbrecht et al., Phytophylactica, 22:341-346 (1990), Rosciglione, et al, Phytoparasitica, 17:63-63 (1989), and Tanne, Phytoparasitica, 16:288 (1988)). Specifically, it has been shown that mealybugs transmit grapevine leafroll virus type-3 only and no others. Natural spread of leafroll by insect vectors is rapid in various parts of the world. Prevalence of leafroll worldwide may increase as chemical control of mealybugs becomes more difficult due to the unavailability of effective insecticides.

In view of the serious risk grapevine leafroll virus poses to vineyards and the absence of an effective treatment of it, the need to prevent this affliction continues to exist. The present invention is directed to overcoming this affliction using biotechnology tools and methods to established disease-free grape plants.

Summary of the Invention

In a first aspect, the invention features an isolated grapevine leafroll virus protein or polypeptide selected from the group consisting of: a polyprotein comprising

a proteinase or a methyltransferase; a proteinase; a methyltransferase; a helicase having an amino terminal amino acid sequence consisting of ValGlyGluSer; and a protein consisting of the amino acid sequence of SEQ ID NO: 13.

One preferred protein or polypeptide is a polyprotein having a molecular weight of from 242 to 248 kDa or the polyprotein includes the amino acid sequence of SEQ ID NO: 15.

Another preferred protein is a proteinase that includes the amino acid sequence of SEQ ID NO: 5. Another preferred protein is a methyltransferase that includes the amino acid sequence of SEQ ID NO: 7.

In a second aspect, the invention features an isolated RNA molecule encoding a protein or polypeptide of the first aspect.

In a third aspect, the invention features an isolated DNA molecule that includes the nucleotide sequence of SEQ ID NO: 2.

In a fourth aspect, the invention features an isolated DNA molecule encoding a protein or polypeptide of the first aspect.

In preferred embodiments of the fourth aspect, the protein or polypeptide is a polyprotein having a molecular weight of from 242 to 248 kDa. Preferably, the polyprotein (i) includes the amino acid sequence of SEQ ID NO: 15; (ii) is a proteinase that includes the amino acid sequence of SEQ ID NO: 5; (iii) is a methyltransferase that includes the amino acid sequence of SEQ ID NO: 7; or (iv) is a helicase that includes the amino acid sequence of SEQ ID NO: 9.

In other preferred embodiments of the fourth aspect, the DNA molecule includes the nucleotide sequence of SEQ ID NO: 3, the nucleotide sequence of SEQ ID NO: 4, the nucleotide sequence of SEQ ID NO: 6, or the nucleotide sequence of SEQ ID NO: 8.

In a fifth aspect, the invention features an expression system that includes an expression vector into which is inserted a heterologous DNA molecule of the third or fourth aspect. The heterologous DNA molecule can be inserted in sense orientation or in antisense orientation.

In a sixth aspect, the invention features a host cell transformed with a heterologous DNA molecule of the third or fourth aspect. The host cell can be

selected from the group consisting of *Agrobacterium vitis* and *Agrobacterium tumefaciens*, a grape cell, or a citrus cell.

The DNA molecules of the invention can be used to make transgenic plants or transgenic plant components (e.g., a scion, a rootstock, or a somatic embryo).

The invention features also a method for conferring viral disease resistance on a plant or plant component, by: (a) transforming a plant cell with a DNA molecule according to the third or fourth aspect, which is expressed on the plant or plant component; and (b) regenerating a transgenic plant or transgenic plant component from the plant cell. In preferred embodiments, the plant or plant component is resistant to a grapevine leafroll virus selected from the group consisting of GLRaV-1, GLRaV-2, GLRaV-3, GLRaV-4, GLRaV-5, and GLRaV-6. In a related embodiment, the plant or plant component is resistant to a beet yellows virus, lettuce infectious virus, or citrus tristeza.

In another aspect, the invention features an antibody or binding portion thereof or probe recognizing the protein or polypeptide according to the first aspect.

In a tenth aspect, the invention features a method for detecting a virus in a sample, the method including: (a) contacting a sample with the antibody of claim 31 under conditions that allow for complex formation between the antibody and the virus; and

(b) detecting the complexes as an indication that the virus is present in the sample.

In an eleventh aspect, the invention features a method for detecting a viral nucleic acid molecule in a sample, the method including: (a) contacting a sample with the DNA of the third aspect or a fragment thereof under conditions that allow for complex formation between the DNA and the virus; and (b) detecting the complexes as an indication that the virus is present in the sample.

In a twelfth aspect, the invention features a method for detecting a viral nucleic acid molecule in a sample, the method including: (a) contacting a sample with the DNA of the fourth aspect or a fragment thereof under conditions that allow for complex formation between the DNA and the virus; and (b) detecting the complexes as an indication that the virus is present in the sample.

By "plant cell" is meant any self-propagating cell bounded by a semi-permeable membrane and containing a plastid. A plant cell, as used herein, is obtained from, without limitation, seeds, suspension cultures, embryos, meristematic regions, callus tissue, protoplasts, leaves, roots, shoots, somatic and zygotic embryos, as well as any part of a reproductive or vegetative tissue or organ.

By "plant component" is meant a part, segment, or organ obtained from an intact plant or plant cell. Exemplary plant components include, without limitation, somatic embryos, leaves, fruits, scions and rootstocks.

By "transgenic" is meant any cell which includes a nucleic acid molecule (for example, a DNA sequence) which is inserted by artifice into a cell and becomes part of the genome of the organism (in either an integrated or extrachromosomal fashion for example, a viral expression construct which includes a subgenomic promoter) which develops from that cell. As used herein, the transgenic organisms are generally transgenic grapevines or grapevine components and the nucleic acid molecule (for example, a transgene) is inserted by artifice into the nuclear or plastidic compartments of the plant cell.

By "transgene" is meant any piece of a nucleic acid molecule (for example, DNA) which is inserted by artifice into a cell, and becomes part of the organism (integrated into the genome or maintained extrachromosomally) which develops from that cell. Such a transgene may include a gene which is partly or entirely heterologous (i.e., foreign) to the transgenic organism, or may represent a gene homologous to an endogenous gene of the organism.

Grapevine leafroll virus resistant transgenic variants of the current commercial grape cultivars and rootstocks allows for more control of the virus while retaining the varietal characteristics of specific cultivars. Furthermore, these variants permit control of GLRaV transmitted either by contaminated scions or rootstocks or other means. In this manner, as well as others, the interests of the environment and the economics of grape cultivation and wine making are all benefited by the present invention.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

Brief Description of the Drawings

Figure 1 shows the genome organization of GLRaV-3 in comparison with the genome organization of GLRaV-2, another closterovirus associated with leafroll disease.

Figure 2 shows the nucleic acid sequence of the GLRaV-3 genomic sequence (SEQ ID NO: 1).

Figure 3 shows the nucleic acid sequence of the 5' untranslated region of GLRaV-3 (SEQ ID NO: 2).

Figure 4 shows the nucleic acid sequence of the ORF 1a (SEQ ID NO: 3).

Figure 5 shows the nucleic acid sequence of the proteinase encoded by ORF 1a (SEQ ID NO: 4).

Figure 6 shows the amino acid sequence of the proteinase encoded by the DNA sequence of ORF 1a (SEQ ID NO: 5).

Figure 7 shows the nucleic acid sequence of the methyltransferase encoded by ORF 1a (SEQ ID NO: 6).

Figure 8 shows the amino acid sequence of the methyltransferase encoded by ORF 1a (SEQ ID NO: 7).

Figure 9 shows the amino acid alignment of various closterovirus methyltransferases.

Figure 10 shows the nucleic acid sequence of the helicase encoded by ORF 1a (SEQ ID NO: 8).

Figure 11 shows the amino acid sequence of the helicase encoded by ORF 1a (SEQ ID NO: 9).

Figure 12 shows the nucleic acid sequence of ORF 1b (SEQ ID NO: 10).

Figure 13 shows the amino acid sequence of the polypeptide encoded by ORF 1b (SEQ ID NO: 11).

Figure 14 shows the nucleic acid sequence of ORF 11 of the present invention (SEQ ID NO: 12).

Figure 15 shows the amino acid sequence of the protein encoded by ORF 11 of the present invention (SEQ ID NO: 13).

Figure 16 shows the amino acid sequence listing of the protein encoded by ORF 1a (SEQ ID NO: 15).

Figure 17 shows the nucleic acid sequence of the 3' untranslated region of GLRaV-3 (SEQ ID NO: 14).

Detailed Description of the Invention

The present invention relates to isolated DNA molecules encoding proteins or polypeptides of grapevine leafroll virus (type 3) ("GLRaV-3") as well as the 5' untranslated and 3' untranslated regions associated therewith. Applicants have completely sequenced the entire GLRaV-3 genome, which contains 13 open reading frames ("ORFs") as compared to the genome of GLRaV-2 (Figure 1). The DNA molecule for the entire GLRaV-3 genome has a nucleotide sequence corresponding to SEQ ID NO: 1 as given in Figure 2.

A 5' untranslated region ("UTR") extends from nucleotides 1-158 of SEQ ID NO: 1 and is listed separately as SEQ ID NO: 2, as shown in Figure 3. The first ORF appearing near the 5' end of the complete GLRaV-3 genome is ORF 1a. The DNA molecule encoding ORF 1a extends from nucleotides 159-6872 of SEQ ID NO: 1 and has a nucleic acid sequence corresponding to SEQ ID NO: 3, as shown in Figure 4. This sequence encodes for a large, GLRaV-3 polyprotein having a molecular weight of about 242-248 kDa, more preferably 245.2 kDa. It is believed this DNA molecule encodes a large, GLRaV-3 polyprotein containing the conserved domains of a proteinase, a methyltransferase, and a helicase.

The proteinase domain found in ORF 1a is encoded by nucleotides 411-770 of SEQ ID NO: 1 and has a nucleic acid sequence comprising SEQ ID NO: 4, as shown in Figure 5. The proteinase domain has an amino acid sequence comprising SEQ ID NO: 5, as given in Figure 6, and is similar to that described for Hepatitis C virus (Hijikata et al., Proc. Natl. Acad. Sci. USA 90:10773-10777 (1993), which is hereby incorporated by reference).

The methyltransferase domain found in ORF 1a is encoded by nucleotides 1536-2351 of SEQ ID NO: 1 and as has a nucleic acid sequence comprising SEQ ID NO: 6, as shown in Figure 7. The methyltransferase domain has an amino acid

sequence comprising SEQ ID NO: 7, as shown in Figure 8. As shown in Figure 9, the methyltransferase domain is similar to methyltransferase domains of other closteroviruses.

The helicase domain found in ORF 1a is encoded by nucleotides 5922-6794 of SEQ ID NO: 1 and has a nucleic acid sequence comprising SEQ ID NO: 8, as shown in Figure 10. The helicase domain has an amino acid sequence comprising SEQ ID NO: 9, as shown in Figure 11.

Another open reading frame of the present invention is found within the GLRaV-3 genome and is designated ORF 1b. This open reading frame is believed to encode a RNA-dependent RNA-polymerase ("RdRp"). The DNA molecule encoding ORF 1b extends from nucleotides 6877-8475 of SEQ ID NO: 1 and has a nucleic acid sequence corresponding to SEQ ID NO: 10, as shown in Figure 12.

The RdRp encoded by the DNA molecule of SEQ ID NO: 10 has an amino acid sequence corresponding to SEQ ID NO: 11, as shown in Figure 13. The protein has a molecular weight of about 58 kDa to 64 kDa, with 61 kDa being most preferred.

Additional ORFs found in GLRaV-3 genome (SEQ ID NO: 1) are as follows: ORF 2 comprises nucleotides 8708-8863; ORF 3 comprises nucleotides 9930-10067; ORF 4 comprises nucleotides 10086-11735; ORF 5 comprises nucleotides 11728-13179; ORF 6 comprises nucleotides 13269-14210; ORF 7 comprises nucleotides 14273-15706; ORF 8 comprises nucleotides 15717-16274; ORF 9 comprises nucleotides 16271-16804; and ORF 10 comprises nucleotides 16811-17350.

ORF 11, which is found in the GLRaV-3 genome (SEQ ID NO: 1) at nucleotides 17353-17463, is given herein as SEQ ID NO: 12 and shown in Figure 14. The ORF encodes a protein having about 36 amino acids (SEQ ID NO:13), which is shown in Figure 15.

ORF 12 is found in the GLRaV-3 genome (SEQ ID NO: 1) at nucleotides 17460-17642. Afterwards, a 3' untranslated regions is observed at nucleotides 17643-17919 of SEQ ID NO: 1.

Also encompassed by the present invention are fragments of the DNA molecules of the present invention. Suitable fragments capable of imparting viral

resistance to plants and plant components are constructed by using appropriate restriction sites, revealed by inspection of the DNA molecule's sequence, to: (i) insert an interposon (Felley et al., Gene, 52:147-15 (1987)) such that truncated forms of the GLRaV-3 polypeptide or protein, lacking various amounts of the C-terminus, can be produced or (ii) delete various internal portions of the protein. Alternatively, the sequence can be used to amplify any portion of the coding region, such that it can be cloned into a vector supplying both transcription and translation start signals. In addition, the 5' untranslated region, or any other portion of the genome, can also be used and expressed either in a sense or antisense to effect viral control within the plant.

Variants may also (or alternatively) be modified by, for example, the deletion or addition of nucleotides that have minimal influence on the properties, secondary structure and hydropathic nature of the encoded polypeptide. For example, the nucleotides encoding a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein that co-translationally or post-translationally directs transfer of the protein to a particular site or organelle. The nucleotide sequence may also be altered so that the encoded polypeptide is conjugated to a linker or other sequence for ease of synthesis, purification, or identification thereof.

The grapevine leafroll virus proteins or polypeptides of the invention are preferably produced in purified form (preferably, at least about 80%, more preferably 90%, pure) by conventional techniques. For example, the protein or polypeptide of the invention is isolated by lysing and sonication. After washing, the pellet is resuspended in buffer containing a suitable buffer such as Tris-HCl. During dialysis, a precipitate forms from this protein solution. The solution is centrifuged, and the pellet is washed and resuspended in the buffer containing said suitable buffer. Proteins are resolved by electrophoresis through a SDS 12% polyacrylamide gel.

Any of the DNA molecules described herein can be incorporated in cells using conventional recombinant DNA technology. It is not necessary for the DNA molecules to be expressed in a manner that results in protein production in order to be within the scope of the present invention. For example, the introduced DNA molecule may express 158 nucleotides of 5' untranslated region. Furthermore, the skilled

artisan may take any of the DNA sequences included herein and may place these sequences in a manner to result in antisense expression, frame shift mutations, or any other manner available to the skilled artisan that results in mRNA production without facilitating translation.

Generally, a DNA molecule to be expressed involves inserting said molecule into an expression system to which the DNA molecule is heterologous (i.e., not normally present). The heterologous DNA molecule is inserted into the expression system or vector in proper sense orientation and correct reading frame. As stated previously, it may also be desired to place the DNA molecule in a orientation that results in a incorrect reading frame. Regardless of reading frame preference, the vector contains the necessary elements for the transcription and translation of the inserted protein-coding sequences.

U.S. Patent No. 4,237,224 to Cohen and Boyer, hereby incorporated by reference, describes the production of expression systems in the form of recombinant plasmids using restriction enzyme cleavage and ligation with DNA ligase. These recombinant plasmids are then introduced by means of transformation and replicated in unicellular cultures including prokaryotic organisms and eukaryotic cells grown in tissue culture.

Recombinant genes may also be introduced into viruses, such as vaccinia virus. Recombinant viruses can be generated by transfection of plasmids into cells infected with virus.

Suitable vectors include, but are not limited to, the following viral vectors such as lambda vector system gt11, gt WES.tB, Charon 4, and plasmid vectors such as pBR322, pBR325, pACYC177, pACYC184, pUC8, pUC9, pUC18, pUC19, pLG339, pR290, pKC37, pKC101, SV 40, pBluescript II SK +/- or KS +/- (see "Stratagene Cloning Systems" Catalog (1993) from Stratagene, La Jolla, CA, hereby incorporated by reference), pQE, pIH821, pGEX, pET series (see Studier et. al., Gene Expression Technology, vol. 185 (1990), hereby incorporated by reference), and any derivatives thereof.

Recombinant molecules can be introduced into cells via transformation, transduction, conjugation, mobilization, electroporation, and the like. The DNA

sequences are cloned into the vector using standard cloning procedures in the art, as described by Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Springs Laboratory, Cold Springs Harbor, New York (1982), hereby incorporated by reference.

A variety of host-vector systems may be utilized to express the protein-encoding sequence(s). Primarily, the vector system must be compatible with the host cell used. Host-vector systems include but are not limited to the following: bacteria transformed with bacteriophage DNA, plasmid DNA, or cosmid DNA; microorganisms such as yeast containing yeast vectors; mammalian cell systems infected with virus (e.g., vaccinia virus, adenovirus, etc.); insect cell systems infected with virus (e.g., baculovirus); and plant cells infected by bacteria or transformed via particle bombardment (i.e. biolistics). The expression elements of these vectors vary in their strength and specificities. Depending upon the host-vector system utilized, any one of a number of suitable transcription and translation elements can be used.

Different genetic signals and processing events control many levels of gene expression (e.g., DNA transcription and messenger RNA ("mRNA") translation). Transcription of DNA is dependent upon the presence of a promoter which is a DNA sequence that directs the binding of RNA polymerase and thereby promotes mRNA synthesis. The DNA sequences of eukaryotic promoters differ from those of prokaryotic promoters. Furthermore, eukaryotic promotors and accompanying genetic signals may not be recognized in or may not function in a prokaryotic system, and, further, prokaryotic promotors may not be recognized and may not function in eukaryotic cells.

Similarly, translation of mRNA in prokaryotes depends upon the presence of the proper prokaryotic signals which may differ from those of eukaryotes. Efficient translation of mRNA in prokaryotes may require a ribosome binding site called the Shine-Dalgarno ("SD") sequence on the mRNA. For a review on maximizing gene expression, see Roberts and Lauer, Methods in Enzymology, 68:473 (1979), hereby incorporated by reference.

Promoters vary in their "strength" (i.e. their ability to promote transcription). For the purposes of expressing a cloned gene, it may be desirable to use strong

promoters in order to obtain a high level of transcription and, hence, expression of the gene. It may also be advantageous, however, to use weak promoters and/or to select plants expressing the transgene at low levels. Depending upon the host cell system utilized, any one of a number of suitable promoters may be used. For instance, when cloning in *E. coli*, its bacteriophages, or plasmids, promoters such as the T7 phage promoter, *lac* promoter, *trp* promoter, *recA* promoter, ribosomal RNA promoter, the P_R and P_L promoters of coliphage lambda and others, including but not limited, to *lac*UV5, *omp*F, *bla*, *lpp*, and the like, may be used to direct high levels of transcription of adjacent DNA segments. Additionally, a hybrid *trp-lac*UV5 (*tac*) promoter or other *E. coli* promoters produced by recombinant DNA or other synthetic DNA techniques may be used to provide for transcription of the inserted gene.

Bacterial host cell strains and expression vectors may be chosen which inhibit the action of the promoter unless specifically induced. In certain operons, the addition of specific inducers may be necessary for efficient transcription of the inserted DNA. For example, the *lac* operon is induced by the addition of lactose or IPTG (isopropylthio-beta-D-galactoside). A variety of other operons, such as *trp*, *pro*, etc., are under different controls.

Specific initiation signals may also be required for efficient gene transcription and translation in prokaryotic cells. These transcription and translation initiation signals may vary in "strength" as measured by the quantity of gene specific messenger RNA and protein synthesized, respectively. The DNA expression vector, which contains a promoter, may also contain any combination of various transcription and/or translation initiation signals. All of these techniques are well known to the artisan skilled in the art of molecular biology.

Once the isolated DNA molecules derived from GLRaV-3, as described above, have been cloned into an expression system, they are ready to be incorporated into a host cell. Such incorporation can be carried out by the various forms of transformation noted above, depending upon the vector/host cell system. Suitable host cells include, but are not limited to, bacteria, virus, yeast, mammalian cells, insect, plant, and the like.

The present invention also relates to RNA molecules which encode the various GLRaV-3 proteins or polypeptides described above. The transcripts can be synthesized using the host cells of the present invention by any of the conventional techniques. The mRNA can be translated either *in vitro* or *in vivo*. Cell-free systems typically include wheat-germ or reticulocyte extracts. *In vivo* translation can be effected, for example, by microinjection into frog oocytes.

One aspect of the present invention involves using one or more of the above DNA molecules encoding the various proteins or polypeptides of GLRaV-3 to transform plants in order to impart viral resistance to the plants. Most preferred are those DNA molecules as described in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, and SEQ ID NO: 12. In some cases, the DNA molecules listed herein can also be translated into protein. Those protein sequences most preferred include those listed herein as SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, and SEQ ID: 15. An additional aspect is the use of either the 5' untranslated region (SEQ ID NO: 2) or the 3' untranslated region (SEQ ID NO: 14) to impart viral resistance in plants. The mechanism by which resistance is imparted in not known. In one hypothetical mechanism, the transformed plant can express, e.g., the GLRaV-3 helicase or polypeptide thereof, and, when the transformed plant is inoculated by a grapevine leafroll virus, such as GLRaV1, GLRaV2, GLRav3, GLRaV4, GLRaV5, or GLRaV6, or combinations of these, or beet yellows virus, lettuce infectious virus, or citrus tristeza, the expressed GLRaV-3 helicase or polypeptide disrupts pathogenesis of the virus.

In this aspect of the present invention the subject DNA molecule incorporated in the plant can be constitutively expressed. Alternatively, expression can be regulated by a promoter which is activated by the presence of grapevine leafroll virus. Suitable promoters for these purposes include those from genes expressed in response to grapevine leafroll virus infiltration.

Any of the isolated DNA molecules described herein can be utilized to impart grapevine leafroll resistance for a wide variety of grapevine plants. Methods for evaluating the resistance of a plant to viral disease are well known in the art. For

example, the level of resistance to viral disease may be determined by comparing physical features and characteristics.

The DNA molecules are particularly well suited to imparting resistance to *Vitis* scion or rootstock cultivars. Scion cultivars which can be protected include those commonly referred to as Table on Raisin Grapes, such as Alden, Almeria, Anab-E-Shahi, Autumn Black, Beauty Seedless, Black Corinth, Black Damascus, Black Malvoisie, Black Prince, Blackrose, Bronx Seedless, Burgrave, Calmeria, Campbell Early, Canner, Cardinal, Catawba, Christmas, Concord, Dattier, Delight, Diamond, Dizmar, Duchess, Early Muscat, Emerald Seedless, Emperor, Exotic, Ferdinand de Lesseps, Fiesta, Flame seedless, Flame Tokay, Gasconade, Gold, Himrod, Hunisa, Hussiene, Isabella, Italia, July Muscat, Khandahar, Katta, Kourgane, Kishmishi, Loose Perlette, Malaga, Monukka, Muscat of Alexandria, Muscat Flame, Muscat Hamburg, New York Muscat, Niabell, Niagara, Olivette blanche, Ontario, Pierce, Queen, Red Malaga, Ribier, Rish Baba, Romulus, Ruby Seedless, Schuyler, Seneca, Suavis (IP 365), Thompson seedless, and Thomuscat. They also include those used in wine production, such as Aleatico, Alicante Bouschet, Aligote, Alvarelhao, Aramon, Baco blanc (22A), Burger, Cabernet franc, Cabernet, Sauvignon, Calzin, Carignane, Charbono, Chardonnay, Chasselas dore, Chenin blanc, Clairette blanche, Early Burgundy, Emerald Riesling, Feher Szagos, Fernao Pires, Flora, French Colombard, Fresia, Furmint, Gamay, Gewurztraminer, Grand noir, Gray Riesling, Green Hungarian, Green Veltliner, Grenache, Grillo, Helena, Inzolia, Lagrein, Lambrusco de Salamino, Malbec, Malvasia bianca, Mataro, Melon, Merlot, Meunier, Mission, Montua de Pilas, Muscadelle du Bordelais, Muscat blanc, Muscat Ottonel, Muscat Saint-Vallier, Nebbiolo, Nebbiolo fino, Nebbiolo Lampia, Orange Muscat, Palomino, Pedro Ximenes, Petit Bouschet, Petite Sirah, Peverella, Pinot noir, Pinot Saint-George, Primitivo di Gioa, Red Veltliner, Refosco, Rkatsiteli, Royalty, Rubired, Ruby Cabernet, Saint-Emilion, Saint Macaire, Salvador, Sangiovese, Sauvignon blanc, Sauvignon gris, Sauvignon vert, Scarlet, Seibel 5279, Seibel 9110, Seibel 13053, Semillon, Servant, Shiraz, Souzao, Sultana Crimson, Sylvaner, Tannat, Teroldico, Tinta Madeira, Tinto cao, Touriga, Traminer, Trebbiano Toscano, Trousseau, Valdepenas, Viognier, Walschriesling, White Riesling, and Zinfandel.

Rootstock cultivars which can be protected include Couderc 1202, Couderc 1613, Couderc 1616, Couderc 3309, Dog Ridge, Foex 33 EM, Freedom, Ganzin 1 (A x R #1), Harmony, Kober 5BB, LN33, Millardet & de Grasset 41B, Millardet & de Grasset 420A, Millardet & de Grasset 101-14, Oppenheim 4 (SO4), Paulsen 775, Paulsen 1045, Paulsen 1103, Richter 99, Richter 110, Riparia Gloire, Ruggeri 225, Saint-George, Salt Creek, Teleki 5A, *Vitis rupestris Constantia*, *Vitis california*, and *Vitis girdiana*.

There exists an extensive similarity in both the methyltransferase and helicase sequence regions of GLRaV-3 and the respective methyltransferase and helicase sequences of other closteroviruses, such as Beet yellows virus, Citris tristeza virus, and lettuce infectious yellow virus. Consequently, the DNA molecules coding for GLRaV-3 methyltransferase or helicase can also be used to produce transgenic cultivars other than grape, such as lettuce, beets, citrus and the like, which are resistant to closteroviruses other than grapevine leafroll, such as tristeza virus. These include cultivars of lemon, lime, orange, grapefruit, pineapple, tangerine, and the like, such as Joppa, Maltaise Ovale, Parson (Parson Brown), Pera, Pineapple, Queen, Shamouti, Valencia, Tenerife, Imperial Doblefina, Washington Sanguine, Moro, Sanguinello Moscato, Spanish Sanguinelli, Tarocco, Atwood, Australian, Bahia, Baiana, Cram, Dalmau, Eddy, Fisher, Frost Washington, Gillette, LengNavelina, Washington, Satsuma Mandarin, Dancy, Robinson, Ponkan, Duncan, Marsh, Pink Marsh, Ruby Red, Red Seedless, Smooth Seville, Orlando Tangelo, Eureka, Lisbon, Meyer Lemon, Rough Lemon, Sour Orange, Persian Lime, West Indian Lime, Bears, Sweet Lime, Troyer Citrange, and Citrus trifoliata.

Plant tissue suitable for transformation include leaf tissue, root tissue, meristems, zygotic and somatic embryos, anthers, and the like. It is particularly preferred to utilize embryos obtained from anther cultures. All of these tissues can be transformed using techniques well known to the skilled artisan. For additional information, WO 97/22700 is incorporated herein by reference.

The expression system of the present invention can be used to transform virtually any plant tissue under suitable conditions. Tissue cells transformed in accordance with the present invention can be grown *in vitro* in a suitable medium to

impart grapevine leafroll virus resistance, as well as beet yellows virus resistance, *Citris tristeza* virus resistance, and lettuce infectious yellows virus resistance. Transformed cells can be regenerated into whole plants such that the protein or polypeptide imparts resistance to grapevine leafroll virus in the intact transgenic plants. In either case, the plant cells transformed with the recombinant DNA expression system of the present invention are grown and caused to express a DNA molecule corresponding to those taught herein, thus, imparting viral resistance.

One technique of transforming plants with the DNA molecules in accordance with the present invention is by contacting the tissue of such plants with an inoculum of a bacteria transformed with a vector comprising a gene in accordance with the present invention which imparts grapevine leafroll resistance. Generally, this procedure involves inoculating the plant tissue with a suspension of bacteria and incubating the tissue for 48 to 72 hours on regeneration medium without antibiotics at 25-28 C.

Bacteria from the genus *Agrobacterium* can be utilized to transform plant cells. Suitable species of such bacterium include *Agrobacterium tumefaciens* and *Agrobacterium rhizogenes*. *Agrobacterium tumefaciens* (e.g., strains C58, LBA4404, or EHA105) is particularly useful due to its well-known ability to transform plants.

Another approach to transforming plant cells with a gene which imparts resistance to pathogens is particle bombardment (also known as biolistic transformation) of the host cell. This can be accomplished in one of several ways, such as those disclosed in U.S. Patent Nos. 4,945,050, 5,036,006, and 5,100,792, all to Sanford et al., and in Emerschad et al., Plant Cell Reports, 14:6-12 (1995), which are hereby incorporated by reference. When inert particles are utilized, the vector can be introduced into the cell by coating the particles with the vector containing the heterologous DNA. Alternatively, the target cell can be surrounded by the vector so that the vector is carried into the cell by the wake of the particle. Biologically active particles (e.g., dried bacterial cells containing the vector and heterologous DNA) can also be propelled into plant cells.

Once grape plant tissue is transformed in accordance with the present invention, it is regenerated to form a transgenic grape plant. Generally, regeneration

is accomplished by culturing transformed tissue on medium containing the appropriate growth regulators and nutrients to allow for the initiation of shoot meristems. Appropriate antibiotics are added to the regeneration medium to inhibit the growth of *Agrobacterium* and to select for the development of transformed cells. Following shoot initiation, shoots are allowed to develop tissue culture and are screened for marker gene activity.

The DNA molecules of the present invention can be made capable of transcription to a messenger RNA, which, although encoding for a GLRaV-3 protein or polypeptide, does not translate to the protein. This is known as RNA-mediated resistance. When a *Vitis* scion or rootstock cultivar is transformed with such a DNA molecule, the DNA molecule can be transcribed under conditions effective to maintain the messenger RNA in the plant cell at low level density readings. Density readings of between 15 and 50, using a Hewlet ScanJet and Image Analysis Program having default settings, are preferred.

The grapevine leafroll virus proteins or polypeptides can also be used to raise antibodies or binding portions thereof or probes. The antibodies can be monoclonal or polyclonal. A description of the theoretical basis and practical methodology of fusing such cells is set forth in Kohler and Milstein, Nature, 256:495 (1975), and Milstein and Kohler, Eur. J. Immunol., 6:511 (1976), hereby incorporated by reference. Procedures for raising polyclonal antibodies are also well known to the skilled artisan. This and other procedures for raising polyclonal antibodies are disclosed in Harlow et. al., editors, Antibodies: A Laboratory Manual (1988), which is hereby incorporated by reference.

In addition to utilizing whole antibodies, binding portions of such antibodies can be used. Such binding portions include Fab fragments, $F(ab')_2$ fragments, and Fv fragments. These antibody fragments can be made by conventional procedures, such as proteolytic fragmentation procedures, as described in Goding, Monoclonal Antibodies: Principles and Practice, New York: Academic Press, pp. 98-118 (1983), hereby incorporated by reference.

The present invention also relates to probes found either in nature or prepared synthetically by recombinant DNA procedures or other biological procedures.

Suitable probes are molecules which bind to grapevine leafroll viral antigens identified by the monoclonal antibodies of the present invention. Such probes can be, for example, proteins, peptides, lectins, or nucleic acid probes.

The antibodies or binding portions thereof or probes can be administered to grapevine leafroll virus infected scion cultivars or rootstock cultivars. Alternatively, at least the binding portions of these antibodies can be sequenced, and the encoding DNA synthesized. The encoding DNA molecule can be used to transform plants together with a promoter which causes expression of the encoded antibody when the plant is infected by grapevine leafroll virus. In either case, the antibody or binding portion thereof or probe will bind to the virus and help prevent the usual viral response.

Antibodies raised against the GLRaV-3 proteins or polypeptides of the present invention or binding portions of these antibodies can be utilized in a method for detection of grapevine leafroll virus in a sample of tissue, such as tissue from a grape scion or rootstock. Antibodies or binding portions thereof suitable for use in the detection method include those raised against a proteinase, a methyltransferase, a helicase, and a protein having a sequence according to SEQ ID NO: 13 in accordance with the present invention. Any reaction of the sample with the antibody is detected using an assay system which indicates the presence of grapevine leafroll virus in the sample. A variety of assay systems can be employed, such as enzyme-linked immunosorbent assays, radioimmunoassays, gel diffusion precipitin reaction assays, immunodiffusion assays, agglutination assays, fluorescent immunoassays, protein A immunoassays, or immunoelectrophoresis assays.

The DNA sequences of the present invention can also be used to clone additional fragments having similar sequences. By "similar sequences" is meant a protein or nucleic acid molecule exhibiting 70%, preferably 80%, and most preferably 90% identity to a reference amino acid sequence or nucleic acid sequence. For proteins, the length of comparison sequences will generally be at least 15 amino acids, preferably at least 20 amino acids, more preferably at least 25 amino acids, amd most preferably 35 amino acids or greater. For nucleic acids, the length of comparison sequences will generally be at least 50 nucleotides, preferably at least 60 nucleotides,

more preferably at least 75 nucleotides, and most preferably 110 nucleotides or greater.

Sequence identity, at the amino acid levels, is typically measured using sequence analysis software (for example, Sequence Analyis Software Package of the Genetics Computer Group, Univerity of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705, BLAST, or PILEUP/PRETTYBOX prgrams). Such software matches identical or similar sequences by assigning degrees of homology to various substitutions, deletions, and/or other modifications.

The present invention also includes nucleic acids that selectively hybridize to GLRaV-3 sequences of the present invention. Hybridization may involve Southern analysis (Southern Blotting), a method by which the presence of DNA sequences in a target nucleic acid mixture are identified by hybridization to a labeled oligonucleotide or DNA fragment probe. Southern analysis typically involves electrophoretic separation of DNA digests on agarose gels, denaturation of the DNA after electrophoretic separation, and transfer of the DNA to nitrocellulose, nylon, or another suitable membrane support for analysis with a radiolabeled, biotinylated, or enzyme-labeled probe as described in Sambrook et al., (1989) <u>Molecular Cloning</u>, 2nd edition , Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.

Hybridization often includes the use of a probe. It is generally preferred that a probe of at least 20 nucleotides in length be used, preferably at least 50 nucleotides, more preferably at least about 100 nucleotides.

A nucleic acid can hybridize under moderate stringency conditions or high stringency conditions to a nucleic acid disclosed herein. High stringency conditions are used to identify nucleic acids that have a high degree of homology or sequence identity to the probe. High stringency conditions can include the use of a denaturing agent such as formamide during hybridization, e.g., 50% formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM NaCl, and 75 mM sodium citrate at 42°C. Another example is the use of 50% formamide, 5X SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5x Denharts solution, sonicated salmon sperm DNA (50 ug/mL) 0.1% SDS, and 10%

dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC and 0.1% SDS. Alternatively, low ionic strength washes and high temperature can be employed for wasbing.

Moderate stringency conditions are hybridization conditions used to identifiy nucleic acids that have less homology or identity to the probe than do nucleic acids under high stringency. All of these techniques are well known to the artisan skilled in molecular biology.

The following examples are provided to illustrate embodiments of the present invention and are by no means intended to limit its scope.

Examples

The examples cited herein incorporate by reference Examples 1-12, and Examples 14-18 in their entirety from WO 97/22700, published 26 June, 1997, which is based on U.S. Application 60/009,008 filed 21 December 1995.

Example 1: Nucleotide Sequence and Open Reading Frames

Cloning and sequencing of the GLRaV-3 genomic DNA was performed exactly as described in WO 97/22700, published 26 June 1997 except as follows.

The genome of GLRaV-3 was determined after the additional 4,765 nucleotides on the 5' terminal portion were obtained and sequenced. The complete genome of GLRaV-3 contains 17,919 nucleotides and contained 13 ORFs with a 5' untranslated region of 158 nucleotides and a 3' untranslated region of 276 nucleotides (Figure 1). The ORF1a, containing 6,714 nucleotides, encoded a large polyprotein with a *Mr* of 245,277. With a +1 frameshift mechanism, it is also possible to produce a large fusion protein (from ORF 1a and ORF 1b) of Mr of 305,955. Surprisingly, GLRAV-3 did not contain a papain-like cysteine proteinase; instead, a proteinase domain similar to the hepatitis C virus (Hijikata et al., Proc. Natl. Acad. Sci. USA 90:10773-10777 (1993), which is hereby incorporated by reference) was identified. The metyltransferase domain and the helicase domain were similar to those of other closteroviruses.

Based upon the original partial sequencing of the helicase, database searching indicated that the C-terminal portion of this protein shared significant similarity with the Superfamily 1 helicase of positive-strand RNA viruses. Comparison of the conserved domain region (291 amino acids) showed a 38.4% identity with an additional 19.7% similarity between GLRaV-3 and BYV and a 32.4% identity with an additional 21.1% similarity between GLRaV-3 and LIYV. Six helicase conserved motifs of Superfamily 1 helicase of positive-strand RNA viruses (Hodgman, Nature, 333:22-23 (Erratum 578) (1988) and Koonin et al., Critical Reviews in Biochemistry and Molecular Biology, 28:375-430 (1993), hereby incorporated by reference) were also retained in GLRaV-3. Analysis of the phylogenetic relationship in helicase domains between GLRaV-3 and the other positive-strand RNA viruses placed GLRaV-3 along with the other closteroviruses, including BYV, CTV, and LIYV, into the "tobamo" branch of the alphavirus-like supergroup. Nucleotide ("nt") and amino acid ("aa") sequence similarity was calculated from perfect matches after aligning with the GCG program GAP; the percentages in parentheses are the percentages calculated by the GAP program, which employs a matching table based on evolutionary conservation of amino acids (Devereux et al., Nucleic Acids Res., 12:387-395 (1984), hereby incorporated by reference). The sources for the BYV, CTV, and LIYV sequences were, respectively, Agranovsky et al., Virology 198:311-324 (1994), Karasev et al., Virology 208: 511- (1995), and Klaassen et al, Virology 208:99-110 (1995) and Rappe et al., Virology 199:35-41 (1994), hereby incorporated by reference.

ORF 1b started at nucleotide 6877 of SEQ ID NO: 1 and went to nucleotide 8475 as given in SEQ ID NO: 10 (Figure 12). This portion encoded for a protein having the amino acid sequence listed in SEQ ID NO: 11 (Figure 13). Database screening of this protein revealed a significant similarity to the Supergroup 3 RdRp of the positive-strand RNA viruses. Sequence comparison of GLRaV-3 with BYV, LIYV, and CTV over a 313-amino acid sequence fragment revealed a striking amino acid sequence similarity among eight conserved motifs. The best alignment was with BYV, with 41.2% identity and 19.8% additional similarity while the least alignment was with LIYV, with 35.9% identity and 20.5% additional similarity. Analysis of

phylogenetic relationships of the RdRp domains of the alphavirus-like supergroup viruses again placed GLRaV-3 into a "tobamo" branch along with other closteroviruses, BYV, CTV, BYSV, and LIYV.

ORF 2 through ORF 10 were exactly as described in Example 13 of WO 97/22700, published 26 June 1997.

ORF 11 encoded an unidentified polypeptide having a calculated *Mr* of 3,933.

ORF 12 was exactly as described for ORF 11 in Example 13 of WO 97/22700, published 26 June 1997. After ORF 12, a 3' untranslated region was obtained having the sequence listed in SEQ ID NO: 14.

Other Embodiments

All publications mentioned in this specification are herein incorporated by reference to the same extent as if each independent publication was specifically and individually indicated to be incorporated by reference.

While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications. This application is intended to cover any variations, uses, or adaptations following, in general, the principles of the invention and including such departures from the present disclosure within known or customary practice within the art to which the invention pertains and may be applied to the essential features hereinbefore set forth, and follows in the scope of the appended claims.

What is Claimed:

1. An isolated grapevine leafroll virus protein or polypeptide selected from the group of a polyprotein comprising a proteinase or a methyltransferase; a proteinase; a methyltransferase; a helicase having an amino terminal amino acid sequence of ValGlyGluSer; a protein consisting of the amino acid sequence of SEQ ID NO: 11; and a protein consisting of the amino acid sequence of SEQ ID NO: 13.

2. The isolated protein or polypeptide of claim 1, wherein the protein or polypeptide is a polyprotein having a molecular weight of from 242 to 248 kDa.

3. The isolated protein or polypeptide of claim 2, wherein the polyprotein comprises the amino acid sequence of SEQ ID NO: 15.

4. The isolated protein or polypeptide of claim 1, wherein the proteinase comprises the amino acid sequence of SEQ ID NO: 5.

5. The isolated protein or polypeptide of claim 1, wherein the methyltransferase comprises the amino acid sequence of SEQ ID NO: 7.

6. An isolated RNA molecule encoding a protein or polypeptide of claim 1.

7. An isolated DNA molecule having a nucleotide sequence of SEQ ID NO: 2 or SEQ ID NO: 14, or encoding a protein or polypeptide of claim 1.

8. The isolated DNA molecule of claim 7, wherein the protein or polypeptide is a polyprotein having a molecular weight of from 242 to 248 kDa.

9. The isolated DNA molecule of claim 8, wherein the polyprotein comprises the amino acid sequence of SEQ ID NO: 15.

10. The isolated DNA molecule of claim 9, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 3.

11. The isolated DNA molecule of claim 7, wherein the protein or polypetide is a proteinase comprising the amino acid sequence of SEQ ID NO: 5.

12. The isolated DNA molecule of claim 11, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 4.

13. The isolated DNA molecule of claim 7, wherein the protein or polypeptide is a methyltransferase comprising the amino acid sequence of SEQ ID NO: 7.

14. The isolated DNA molecule of claim 13, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 6.

15. The isolated DNA molecule of claim 7, wherein the protein or poypeptide is a helicase comprising the amino acid sequence of SEQ ID NO: 9.

16. The isolated DNA molecule of claim 15, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 8.

17. The isolated DNA molecule of claim 7, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 10.

18. The isolated DNA molecule of claim 7, wherein the DNA molecule comprises the nucleotide sequence of SEQ ID NO: 12.

19. An expression system comprising an expression vector into which is inserted a heterologous DNA molecule of claim 7.

20. The expression system of claim 19, wherein the heterologous DNA molecule is inserted in sense orientation.

21. The expression system of claim 19, wherein the heterologous DNA molecule is inserted in antisense orientation.

22. A host cell transformed with a heterologous DNA molecule of claim 7.

23. The host cell of claim 22, wherein the host cell is selected from the group of *Agrobacterium vitis* and *Agrobacterium tumefaciens*.

24. The host cell of claim 22, wherein the host cell is a grape cell or a citrus cell.

25. A transgenic plant or transgenic plant component comprising the DNA molecule according to claim 7.

26. The transgenic plant or transgenic plant component of claim 25, wherein said transgenic plant component is a scion.

27. The transgenic plant or transgenic plant component of claim 25, wherein said transgenic plant component is a rootstock.

28. The transgenic plant or transgenic plant component of claim 25, wherein said transgenic plant component is a somatic embryo.

29. A method of conferring viral disease resistance to a plant or plant component, said method comprising the steps of :

(a) transforming a plant cell with a DNA molecule according to claim 7 which is expressed in said plant or plant component; and

(b) regenerating a transgenic plant or transgenic plant component from said plant cell.

30. The method of claim 29, wherein said plant or plant component is resistant to a grapevine leafroll virus selected from the group of GLRaV-1, GLRaV-2, GLRaV-3, GLRaV-4, GLRaV-5, and GLRaV-6.

31. The method of claim 29, wherein said plant or plant component is resistant to a beet yellows virus, lettuce infectious yellows virus, or citrus tristeza virus.

32. An antibody or binding portion thereof or probe recognizing the protein or polypeptide according to claim 1.

33. A method for detecting a virus in a sample, said method comprising:

(a) contacting a sample with the antibody of claim 32 under conditions that allow for complex formation between said antibody and said virus; and

(b) detecting said complexes as an indication that said virus is present in said sample.

34. A method for detecting a viral nucleic acid molecule in a sample, said method comprising:

(a) contacting a sample with the DNA of claim 7 or a fragment thereof under conditions that allow for complex formation between said DNA and said virus; and

(b) detecting said complexes as an indication that said virus is present in said sample.

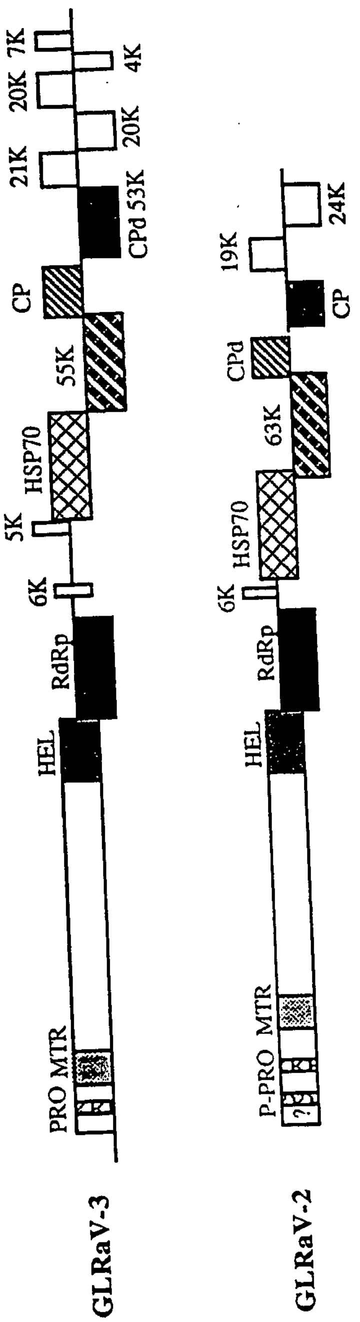
GLRaV-3
PRO MTR
HEL
RdRp
6K
5K
HSP70
55K
CP
CPd 53K
21K
20K
20K
7K
4K
GLRaV-2
P-PRO MTR
HEL
RdRp
6K
HSP70
63K
CPd
CP
19K
24K

Figure 1

ctaagtaaca cctaggaatt tctacctaag attcaacttc tttctttttc tagttttaaa 60
ttttcctgct gtttgaggga agtttgccct tcttcttccg tcgtccttcg taaaccatta 120
tttctatttc ctctcctttt aagtttttaa gtttcgctat ggactacatt cgcccattgc 180
gcgttttctc ctttcctcac gttaataaca ccttggagta cgttaggtac aacaaggcca 240
atggtgatgt aggagctttc ctaaccacca tgaagttcat agggaacgtg aagttgtcgg 300
acttcacacc caggtgcgca gctatgattt acattggaaa gctcaccaaa ggggtgaagc 360
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ttgtcgtaca ctaccaccgg gtagtgccgt atgcccccgt caagcgcgag cagcctaaac 600
cggctgttaa gcaagatgag cagaagccca aacggcaagc gtcacattgg gctgttaagc 660
caacagctgt tggcgtccac gtaccacttc ctaaaaaaca ggaagcactg gagccagcgc 720
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cattcgctaa tgccatgcgg agctgtttca atggaatctt ttccaggagg tgtggtaatg 1680

Figure 2

tgtgcttctt cgatattggg gggagcttca cgtatcatgt caaagctggc catgtgaact 1740
gtcatgtatg caatccagtc ctagacgtta aagatgtgaa gcggagaatc aatgagatcc 1800
tctttctttc cacagctggg ggagattcgt acgtgtccag tgaccttcta actgaagcgg 1860
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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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Figure 2-cont.

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aagaaaaagg agaggcaagt attattatag tggtgattgt ggatccgacg ttgcgaaagt 16680
taagtatatt ttgtctgggg agaatcgagg attggggtgc gtagattcct tgaagctagt 16740
ttgcgtaggt agacaaggag gtggaaacgt actacagcac ctactaatct catctctggg 16800

Figure 2-cont.

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Figure 2-cont.

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ttttcctgct gtttgaggga agtttgccct tcttcttccg tcgtccttcg taaaccatta 120
tttctatttc ctctcctttt aagtttttaa gtttcgct                        158
```

Figure 3

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tacgttaggt acaacaaggc caatggtgat gtaggagctt tcctaaccac catgaagttc 120
atagggaacg tgaagttgtc ggacttcaca cccaggtgcg cagctatgat ttacattgga 180
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cagtacgctg ttgtcagcgg ctcagtcagc gcgctgagag gggatggtaa gaaggtcttg 300
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gcgtcacatt gggctgttaa gccaacagct gttggcgtcc acgtaccact tcctaaaaaa 540
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cggaaaggga aattgtttaa cagggccctt aatgttccta ttgatgtaaa gaacacgttc 720
gtttgggcta aaatctggga tgaagcctct cgtaggagag ggtattttta cgtcaaagat 780
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Figure 4

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cccgtggagt tgttgtacgg taacggtgaa gtttacttgg aagaactcga tacgttggtg 1920
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Figure 4-cont.

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Figure 4-cont.

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Figure 4-cont.

```
gtcagcggct cagtcagcgc gctgagaggg gatggtaaga aggtcttgat ggaggcaagg  60
acctcaactt ccgcaacttc cgacgtgtct gatttcgacg tcgtattcga agctgtttct 120
aatgcattac ttgtcgtaca ctaccaccgg gtagtgccgt atgcccccgt caagcgcgag 180
cagcctaaac cggctgttaa gcaagatgag cagaagccca aacggcaagc gtcacattgg 240
gctgttaagc caacagctgt tggcgtccac gtaccacttc ctaaaaaaca ggaagcactg 300
gagccagcgc aatcagtccc acaacagtcg ttggaggaga aggccgcctt gacgtttggc 360
```

Figure 5

```
VSGSVSALRG DGKKVLMEAR TSTSATSDVS DFDVVFEAVS NALLVVHYHR  50
VVPYAPVKRE QPKPAVKQDE QKPKRQASHW AVKPTAVGVH VPLPKKQEAL 100
EPAQSVPQQS LEEKAALTFG                                  120
```

Figure 6

ctgaagccgc gggaaaggga gaagctgagg gaactctttc cagagctttc gatacagttc 60
tccgactcgg tcaggagtag tcacccattc gctaatgcca tgcggagctg tttcaatgga 120
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tccagtgacc ttctaactga agcggcttca aagtctgtgt cttactgtag tcgagaatcg 360
cagaactgcg attctagagc cgatgcgggt tttatggtgg atgtgtacga tatatccccg 420
cagcaggtag cagaggctat ggataagaag ggtgcgctgg ttttcgacat agctcttatg 480
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cattccttct ctaacgtaag cgggtttttc accttttctt atgtacgcac ttcgtccggg 660
aacgtgttta agctagagta tgagggatac cgttgtggtt accatcatct cactatgtgt 720
agggctcaga agtcacctgg aactgaggtt acgtataggt cgttggtccc gtcgttcgtg 780
ggcaaatcgc tggtgttcat acctgttgta gctggt 816

Figure 7

LKPREREKLR ELFPELSIQF SDSVRSSHPF ANAMRSCFNG IFSRRCGNVC FFDIGGSFTY 60
HVKAGHVNCH VCNPVLDVKD VKRRINEILF LSTAGGDSYV SSDLLTEAAS KSVSYCSRES 120
QNCDSRADAG FMVDVYDISP QQVAEAMDKK GALVFDIALM FPVELLYGNG EVYLEELDTL 180
VKREGDYLAY NVGQCGEMYE HSFSNVSGFF TFSYVRTSSG NVFKLEYEGY RCGYHHLTMC 240
RAQKSPGTEV TYRSLVPSFV GKSLVFIPVV AG 272

Figure 8

```
                                       MT I                             MT Ia              MT II
Consensus#1   ............P.....F.....S.H.....R...N.............D.GG..............H.C.P..D..D..R........

GLRaV2-MTR    MSEATQNSLTRFYPQFELKFSHSSHSDHPAAAASRLLENETLVRLCGNS-VSDIGGCPLFHLHSKTQRRVHVCRPVLDGKDAQRRVVRDLQY
BYV-MTR       MGEAVQSGLTRAYPQFNLSFTHSVYSDHPAAAGSRLLENETLASMAKSS-FSDIGGCPLFHIK-RGSTDYHVCRPIYDMKDAQRRVSRELQA
LIYV-MTR      LSMDEKKMITNLFPDIQMSFNQKSYSNHGVFNAMRACENFYFSRKFKNSDYIDAGGDVVSTLRSK-NHNVHICSPRLDLKDAARHIQRATVI
CTV-MTR       MSENQQVMLTRAYPEFNINFIHSVHSDHPVAAGSRALENHLVRKHAGTD-YSDVGGCPLFHLRA-GHSGVHVCRPVYDVKDAHRRVVRHHQL
LCV-MTR       LSTRQKKIVCDLFPHLKFEFKETTQSSHPVFNVVRTVSNFVLYKMQEGRHFVDFGGNIGTVINSE-CDDVHICNPVADSRDAKRHVDNGLFL
GLRaV3-MTR    LKPREREKLRELFPELSIQFSDSVRSSHPFANAMRSCFNGIFSRRCGNVCFFDIGGSFTYHVKAG-HVNCHVCNPVLDVKDVKRRINEILFL

                                    MT IIa        MT III
Consensus#1   .....................C.....C........V.VYD.......AM.............P....................

GLRaV2-MTR    SNVRLG-DDD--KILEGPRN-IDICHYPLGACDHESSAMMMVQVYDASLYEICGAMIKKKSRITYLTMVTPGEFLDGRECVYMESLDCEIEV
BYV-MTR       RGLVENLSRE--QLVEAQAR-VSVCPHTLGNCNVKSDVLIMVQVYDASLNEIASAMVLKESKVAYLTMVTPGELLDEREAFAIDALGCDVVV
LIYV-MTR      DGLKG------------YGETISFCTNKTEDCAVNRDIIIAVEVYDMTLRDMAKAMLSHGSRKFEFSCIIPPEIFTKECNVELYEGRLKV--
CTV-MTR       SKVSLDQSDGVKQVGWTVNT-NSVCGNILGECYHASEAMVMVQVYDVPLRELCRAMINKKTSVCYMTMVTPGELLDARESFFIKDLDCSVEL
LCV-MTR       AKSVG------------VSNNISVCNKLAQHCNHKSDRAVMVEVYDMTLTEMCQAMLAHGTIRLDFILLLPGDLLEDFNTITIFDGGCKI--
GLRaV3-MTR    STAGGDSYVSSDLLTEAASKSVSYCSRESQNCDSRADAGFMVDVYDISPQQVAEAMDKKGALVFDIALMFPVELLYGNGEVYLEELDTLV--

                      MT IV
Consensus#1   ....D...Y.........H.................G..F.............................................

GLRaV2-MTR    DVHADVVMYKFGSSC--YSHKLSIIKDIMTTPYLTLG-GFLFSVEMYEVRMGVNYFKITKSEVSPSISCTKLLRYRRANSDVVKVKLPRFD
BYV-MTR       DTRRDMVQYKFGSSC--YCHKLSNIKSIMLTPAFTFS-GNLFSVEMYENRMGVNYYKITRSAYSPEIRGVKTLRYRRACTEVVQVKLPRFD
LIYV-MTR      TRIGDNVEYYYGSNGETFSHSCQTLKDILSVQVFQFG-GRVFKKTLEHSRGQLHFFSICICEKIEPGSVKLKTYYQRSELDKVTLRIPVKD
CTV-MTR       DPIADRVVYCFNNSA--YTHTYSTICECMRTPCLVVD-GFLFTIEMVSLRCSVNYYCITKSSVCPRISETKRLRYRRCDSDLIRIKIPRYS
LCV-MTR       TKDDDKVYYYYGDAAEAYTHDLNNLRNIMTDNLVCVD-GTAFKKTLETSYGPFRHFSLTKLETFPSGKIEFLTMYDKCEKNKMLVKVPMRN
GLRaV3-MTR    KREGDYLAYNVGQCGEMYEHSFSNVSGFFTFSYVRTSSGNVFKLEYEGYRCGYHHLTMCRAQKSPGTEVTYRSLVPSFVGKSLVFIPVVAG
```

Figure 9

```
gtgggcgaat cgtttaagtc cttcgaatat aagtgctata atgctccccc aggtggcggt   60
aagacgacga cgttagtgga cgaattcgtt aagtcaccca atagcacagc caccattacg  120
gctaatgtgg gaagttctga ggacataaat atggcggtga agaagagaga tccgaatttg  180
gaaggtctca acagtgctac cacagttaac tccagggtgg taaactttat cgtcagggga  240
atgtataaaa gggttttggt ggatgaggtg cacatgatgc atcaaggctt actacaacta  300
ggcgtcttcg caaccggcgc gtcggaaggc ctctttttg gagacataaa tcagatacca   360
ttcataaaca gggagaaggt gtttaggatg gattgtgctg tttttgttcc aaagaaggaa  420
agcgttgtat acacttctaa atcgtacagg tgtccgttag atgtttgcta cttgttgtcc  480
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ataaacgctg acgtgtactt gtgcatgacc cagttggaga agtcggatat gaagaggtcg  660
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ttcagtgatg tggtattgtt taggacgaag aaagccgatg actccctatt cactaaacaa  780
ccgcatatac ttgttggttt gtcgagacac acacgctcac tggtttatgc cgctctgagc  840
tcaaagttgg acgataaggt cggcacatat att                                873
```

Figure 10

```
VGESFKSFEY KCYNAPPGGG KTTTLVDEFV KSPNSTATIT ANVGSSEDIN MAVKKRDPNL   60
EGLNSATTVN SRVVNFIVRG MYKRVLVDEV HMMHQGLLQL GVFATGASEG LFFGDINQIP  120
FINREKVFRM DCAVFVPKKE SVVYTSKSYR CPLDVCYLLS SMTVRGTEKC YPEKVVSGKD  180
KPVVRSLSKR PIGTTDDVAE INADVYLCMT QLEKSDMKRS LKGKGKETPV MTVHEAQGKT  240
FSDVVLFRTK KADDSLFTKQ PHILVGLSRH TRSLVYAALS SKLDDKVGTY I            291
```

Figure 11

```
atgaattttg gaccgacctt cgaaggggag ttggtacgga agataccaac aagtcatttt     60
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Figure 12

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GDDSLIFSRQ PLDIDTSVLS DNFGFDVKIF NQAAPYFCSK FLVQVEDSLF FVPDPLKLFV 420
KFGASKTSDI DLLHEIFQSF VDLSKGFNRE DVIQELAKLV TRKYKHSGWT YSALCVLHVL 480
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Figure 13

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Figure 14

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Figure 15

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Figure 16

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Figure 17

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<210> 4
<211> 360
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 4
gtcagcggct cagtcagcgc gctgagaggg gatggtaaga aggtcttgat ggaggcaagg 60
acctcaactt ccgcaacttc cgacgtgtct gatttcgacg tcgtattcga agctgtttct 120
aatgcattac ttgtcgtaca ctaccaccgg gtagtgccgt atgccccgt caagcgcgag 180
cagcctaaac cggctgttaa gcaagatgag cagaagccca aacggcaagc gtcacattgg 240
gctgttaagc caacagctgt tggcgtccac gtaccacttc ctaaaaaaca ggaagcactg 300
gagccagcgc aatcagtccc acaacagtcg ttggaggaga aggccgcctt gacgtttggc 360

<210> 5
<211> 120
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 5
Val Ser Gly Ser Val Ser Ala Leu Arg Gly Asp Gly Lys Lys Val Leu
1 5 10 15

Met Glu Ala Arg Thr Ser Thr Ser Ala Thr Ser Asp Val Ser Asp Phe
20 25 30

Asp Val Val Phe Glu Ala Val Ser Asn Ala Leu Leu Val Val His Tyr
35 40 45

His Arg Val Val Pro Tyr Ala Pro Val Lys Arg Glu Gln Pro Lys Pro
50 55 60

Ala Val Lys Gln Asp Glu Gln Lys Pro Lys Arg Gln Ala Ser His Trp
65 70 75 80

Ala Val Lys Pro Thr Ala Val Gly Val His Val Pro Leu Pro Lys Lys
85 90 95

Gln Glu Ala Leu Glu Pro Ala Gln Ser Val Pro Gln Gln Ser Leu Glu
100 105 110

Glu Lys Ala Ala Leu Thr Phe Gly
115 120

<210> 6
<211> 816
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 6
ctgaagccgc gggaaaggga gaagctgagg gaactctttc cagagctttc gatacagttc 60
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atcttttcca ggaggtgtgg taatgtgtgc ttcttcgata ttggggggag cttcacgtat 180
catgtcaaag ctggccatgt gaactgtcat gtatgcaatc cagtcctaga cgttaaagat 240
gtgaagcgga gaatcaatga gatcctcttt ctttccacag ctgggggaga ttcgtacgtg 300
tccagtgacc ttctaactga agcggcttca aagtctgtgt cttactgtag tcgagaatcg 360
cagaactgcg attctagagc cgatgcgggt tttatggtgg atgtgtacga tatatccccg 420
cagcaggtag cagaggctat ggataagaag ggtgcgctgg ttttcgacat agctcttatg 480
ttccccgtgg agttgttgta cggtaacggt gaagtttact tggaagaact cgatacgttg 540
gtgaagaggg aaggtgatta cctggcctac aatgttggtc agtgtggtga gatgtatgaa 600
cattccttct ctaacgtaag cgggtttttc accttttctt atgtacgcac ttcgtccggg 660
aacgtgttta agctagagta tgagggatac cgttgtggtt accatcatct cactatgtgt 720
agggctcaga agtcacctgg aactgaggtt acgtataggt cgttggtccc gtcgttcgtg 780
ggcaaatcgc tggtgttcat acctgttgta gctggt 816

<210> 7
<211> 272
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 7
Leu Lys Pro Arg Glu Arg Glu Lys Leu Arg Glu Leu Phe Pro Glu Leu
1 5 10 15

Ser Ile Gln Phe Ser Asp Ser Val Arg Ser Ser His Pro Phe Ala Asn

20 25 30

Ala Met Arg Ser Cys Phe Asn Gly Ile Phe Ser Arg Arg Cys Gly Asn
35 40 45

Val Cys Phe Phe Asp Ile Gly Gly Ser Phe Thr Tyr His Val Lys Ala
50 55 60

Gly His Val Asn Cys His Val Cys Asn Pro Val Leu Asp Val Lys Asp
65 70 75 80

Val Lys Arg Arg Ile Asn Glu Ile Leu Phe Leu Ser Thr Ala Gly Gly
85 90 95

Asp Ser Tyr Val Ser Ser Asp Leu Leu Thr Glu Ala Ala Ser Lys Ser
100 105 110

Val Ser Tyr Cys Ser Arg Glu Ser Gln Asn Cys Asp Ser Arg Ala Asp
115 120 125

Ala Gly Phe Met Val Asp Val Tyr Asp Ile Ser Pro Gln Gln Val Ala
130 135 140

Glu Ala Met Asp Lys Lys Gly Ala Leu Val Phe Asp Ile Ala Leu Met
145 150 155 160

Phe Pro Val Glu Leu Leu Tyr Gly Asn Gly Glu Val Tyr Leu Glu Glu
165 170 175

Leu Asp Thr Leu Val Lys Arg Glu Gly Asp Tyr Leu Ala Tyr Asn Val
180 185 190

Gly Gln Cys Gly Glu Met Tyr Glu His Ser Phe Ser Asn Val Ser Gly
195 200 205

Phe Phe Thr Phe Ser Tyr Val Arg Thr Ser Ser Gly Asn Val Phe Lys
210 215 220

Leu Glu Tyr Glu Gly Tyr Arg Cys Gly Tyr His His Leu Thr Met Cys
225 230 235 240

Arg Ala Gln Lys Ser Pro Gly Thr Glu Val Thr Tyr Arg Ser Leu Val
245 250 255

Pro Ser Phe Val Gly Lys Ser Leu Val Phe Ile Pro Val Val Ala Gly
260 265 270

<210> 8
<211> 873
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 8
gtgggcgaat cgtttaagtc cttcgaatat aagtgctata atgctccccc aggtggcggt 60
aagacgacga cgttagtgga cgaattcgtt aagtcaccca atagcacagc caccattacg 120
gctaatgtgg gaagttctga ggacataaat atggcggtga agaagagaga tccgaatttg 180
gaaggtctca acagtgctac cacagttaac tccagggtgg taaactttat cgtcagggga 240
atgtataaaa gggttttggt ggatgaggtg cacatgatgc atcaaggctt actacaacta 300
ggcgtcttcg caaccggcgc gtcggaaggc ctctttttg gagacataaa tcagatacca 360
ttcataaaca gggagaaggt gtttaggatg gattgtgctg tttttgttcc aaagaaggaa 420
agcgttgtat acacttctaa atcgtacagg tgtccgttag atgtttgcta cttgttgtcc 480
tcaatgaccg taaggggaac ggaaaagtgt taccctgaaa aggtcgttag cggtaaggac 540
aaaccagtag taagatcgct gtccaaaagg ccaattggaa ccactgatga cgtagctgaa 600
ataaacgctg acgtgtactt gtgcatgacc cagttggaga agtcggatat gaagaggtcg 660
ttgaagggaa aaggaaaaga aacaccagtg atgacagtgc atgaagcaca gggaaaaaca 720
ttcagtgatg tggtattgtt taggacgaag aaagccgatg actccctatt cactaaacaa 780
ccgcatatac ttgttggttt gtcgagacac acacgctcac tggtttatgc cgctctgagc 840
tcaaagttgg acgataaggt cggcacatat att 873

<210> 9
<211> 291
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 9
Val Gly Glu Ser Phe Lys Ser Phe Glu Tyr Lys Cys Tyr Asn Ala Pro
1 5 10 15

Pro Gly Gly Gly Lys Thr Thr Thr Leu Val Asp Glu Phe Val Lys Ser
20 25 30

Pro Asn Ser Thr Ala Thr Ile Thr Ala Asn Val Gly Ser Ser Glu Asp
35 40 45

Ile Asn Met Ala Val Lys Lys Arg Asp Pro Asn Leu Glu Gly Leu Asn
50 55 60

Ser Ala Thr Thr Val Asn Ser Arg Val Val Asn Phe Ile Val Arg Gly
65 70 75 80

Met Tyr Lys Arg Val Leu Val Asp Glu Val His Met Met His Gln Gly
85 90 95

Leu Leu Gln Leu Gly Val Phe Ala Thr Gly Ala Ser Glu Gly Leu Phe
100 105 110

Phe Gly Asp Ile Asn Gln Ile Pro Phe Ile Asn Arg Glu Lys Val Phe
115 120 125

Arg Met Asp Cys Ala Val Phe Val Pro Lys Lys Glu Ser Val Val Tyr
130 135 140

Thr Ser Lys Ser Tyr Arg Cys Pro Leu Asp Val Cys Tyr Leu Leu Ser
145 150 155 160

Ser Met Thr Val Arg Gly Thr Glu Lys Cys Tyr Pro Glu Lys Val Val
165 170 175

Ser Gly Lys Asp Lys Pro Val Val Arg Ser Leu Ser Lys Arg Pro Ile
180 185 190

Gly Thr Thr Asp Asp Val Ala Glu Ile Asn Ala Asp Val Tyr Leu Cys
195 200 205

Met Thr Gln Leu Glu Lys Ser Asp Met Lys Arg Ser Leu Lys Gly Lys
210 215 220

Gly Lys Glu Thr Pro Val Met Thr Val His Glu Ala Gln Gly Lys Thr
225 230 235 240

Phe Ser Asp Val Val Leu Phe Arg Thr Lys Lys Ala Asp Asp Ser Leu
245 250 255

Phe Thr Lys Gln Pro His Ile Leu Val Gly Leu Ser Arg His Thr Arg
260 265 270

Ser Leu Val Tyr Ala Ala Leu Ser Ser Lys Leu Asp Asp Lys Val Gly
275 280 285

Thr Tyr Ile
290

<210> 10
<211> 1599
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 10
atgaattttg gaccgacctt cgaaggggag ttggtacgga agataccaac aagtcatttt 60

gtagccgtga atgggtttct cgaggactta ctcgacggtt gtccggcttt cgactatgac 120
ttctttgagg atgatttcga aacttcagat cagtctttcc tcatagaaga tgtgcgcatt 180
tctgaatctt tttctcattt tacgtcgaaa atagaggata ggttttacag ttttattagg 240
tctagcgtag gtttaccaaa gcgcaacacc ttgaagtgta acctcgtcac gtttgaaaat 300
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agccatttgt ccagcaacac gatgttgtta tcagattggt tggacaaaag ggcacctaac 480
gcttacaagt ctctcaagcg ggctttaggt tcgtttgtct ttcatccgtc tatgttgact 540
tcttatacgc tcatggtgaa agcagacgta aaacccaagt tggacaatac gccattgtcg 600
aagtacgtaa cggggcagaa tatagtctac cacgataggt gcgtaactgc gctttttct 660
tgcattttta ctgcgtgcgt agagcgctta aaatacgtag tggacgaaag gtggctcttc 720
taccacggga tggacactgc ggagttggcg gctgcattga ggaacaattt gggggacatc 780
cggcaatact acacctatga actggatatc agtaagtacg acaaatctca gagtgctctc 840
atgaagcagg tggaggagtt gatactcttg acacttggtg ttgatagaga agttttgtct 900
actttctttt gtggtgagta tgatagcgtc gtgagaacga tgacgaagga attggtgttg 960
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gataattttg gttttgacgt aaagattttt aaccaagctg ctccatattt ttgttctaag 1200
tttttagttc aagtcgagga tagtctcttt tttgttcccg atccacttaa actcttcgtt 1260
aagtttggag cttccaaaac ttcagatatc gaccttttac atgagatttt tcaatctttc 1320
gtcgatcttt cgaagggttt caatagagag gacgtcatcc aggaattagc taagctggtg 1380
acgcggaaat ataagcattc gggatggacc tactcggctt tgtgtgtctt gcacgtttta 1440
agtgcaaatt tttcgcagtt ctgtaggtta tattaccaca atagcgtgaa tctcgatgtg 1500
cgccctattc agaggaccga gtcgctttcc ttgctggcct tgaaggcaag aattttaagg 1560
tggaaagctt ctcgttttgc cttttcgata aagaggggt 1599

<210> 11
<211> 533
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 11
Met Asn Phe Gly Pro Thr Phe Glu Gly Glu Leu Val Arg Lys Ile Pro
1 5 10 15

Thr Ser His Phe Val Ala Val Asn Gly Phe Leu Glu Asp Leu Leu Asp
20 25 30

Gly Cys Pro Ala Phe Asp Tyr Asp Phe Phe Glu Asp Asp Phe Glu Thr
35 40 45

Ser Asp Gln Ser Phe Leu Ile Glu Asp Val Arg Ile Ser Glu Ser Phe
50 55 60

Ser His Phe Thr Ser Lys Ile Glu Asp Arg Phe Tyr Ser Phe Ile Arg
65 70 75 80

Ser Ser Val Gly Leu Pro Lys Arg Asn Thr Leu Lys Cys Asn Leu Val
85 90 95

Thr Phe Glu Asn Arg Asn Phe Asn Ala Asp Arg Gly Cys Asn Val Gly
100 105 110

Cys Asp Asp Ser Val Ala His Glu Leu Lys Glu Ile Phe Phe Glu Glu
115 120 125

Val Val Asn Lys Ala Arg Leu Ala Glu Val Thr Glu Ser His Leu Ser
130 135 140

Ser Asn Thr Met Leu Leu Ser Asp Trp Leu Asp Lys Arg Ala Pro Asn
145 150 155 160

Ala Tyr Lys Ser Leu Lys Arg Ala Leu Gly Ser Phe Val Phe His Pro
165 170 175

Ser Met Leu Thr Ser Tyr Thr Leu Met Val Lys Ala Asp Val Lys Pro
180 185 190

Lys Leu Asp Asn Thr Pro Leu Ser Lys Tyr Val Thr Gly Gln Asn Ile
195 200 205

Val Tyr His Asp Arg Cys Val Thr Ala Leu Phe Ser Cys Ile Phe Thr
210 215 220

Ala Cys Val Glu Arg Leu Lys Tyr Val Val Asp Glu Arg Trp Leu Phe
225 230 235 240

Tyr His Gly Met Asp Thr Ala Glu Leu Ala Ala Ala Leu Arg Asn Asn
245 250 255

Leu Gly Asp Ile Arg Gln Tyr Tyr Thr Tyr Glu Leu Asp Ile Ser Lys
260 265 270

Tyr Asp Lys Ser Gln Ser Ala Leu Met Lys Gln Val Glu Glu Leu Ile
275 280 285

Leu Leu Thr Leu Gly Val Asp Arg Glu Val Leu Ser Thr Phe Phe Cys
290 295 300

Gly Glu Tyr Asp Ser Val Val Arg Thr Met Thr Lys Glu Leu Val Leu
305 310 315 320

Ser Val Gly Ser Gln Arg Arg Ser Gly Gly Ala Asn Thr Trp Leu Gly
325 330 335

Asn Ser Leu Val Leu Cys Thr Leu Leu Ser Val Val Leu Arg Gly Leu
340 345 350

Asp Tyr Ser Tyr Ile Val Val Ser Gly Asp Asp Ser Leu Ile Phe Ser
355 360 365

Arg Gln Pro Leu Asp Ile Asp Thr Ser Val Leu Ser Asp Asn Phe Gly
370 375 380

Phe Asp Val Lys Ile Phe Asn Gln Ala Ala Pro Tyr Phe Cys Ser Lys
385 390 395 400

Phe Leu Val Gln Val Glu Asp Ser Leu Phe Phe Val Pro Asp Pro Leu
405 410 415

Lys Leu Phe Val Lys Phe Gly Ala Ser Lys Thr Ser Asp Ile Asp Leu
420 425 430

Leu His Glu Ile Phe Gln Ser Phe Val Asp Leu Ser Lys Gly Phe Asn
435 440 445

Arg Glu Asp Val Ile Gln Glu Leu Ala Lys Leu Val Thr Arg Lys Tyr
450 455 460

Lys His Ser Gly Trp Thr Tyr Ser Ala Leu Cys Val Leu His Val Leu
465 470 475 480

Ser Ala Asn Phe Ser Gln Phe Cys Arg Leu Tyr Tyr His Asn Ser Val
485 490 495

Asn Leu Asp Val Arg Pro Ile Gln Arg Thr Glu Ser Leu Ser Leu Leu
500 505 510

Ala Leu Lys Ala Arg Ile Leu Arg Trp Lys Ala Ser Arg Phe Ala Phe
515 520 525

Ser Ile Lys Arg Gly
530

<210> 12
<211> 111
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 12
atgttatgtt gttcagccag tgtcaaattt tcaaacgggt tacaattatc gctacttatt 60
tgcgcatgtt tgttagcggt gctaattgtt agcttttgta gaaggcgatg a 111

<210> 13
<211> 36
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 13
Met Leu Cys Cys Ser Ala Ser Val Lys Phe Ser Asn Gly Leu Gln Leu
1 5 10 15

Ser Leu Leu Ile Cys Ala Cys Leu Leu Ala Val Leu Ile Val Ser Phe
20 25 30

Cys Arg Arg Arg
35

<210> 14
<211> 279
<212> DNA
<213> grapevine leafroll-associated virus 3

<400> 14
aaaaatcctt caataaattt gaaataaaca aaagtaagaa aaatgaaata attaggctag 60
tctttttgtt cgtctttcgc ttttgtagaa taggttttat ttcgaggtaa gatgactaaa 120
ctttacctca cggtttaata ctctgatatt tgtaaaatta gtccgtaaag tcgatagtga 180
tattatatta gtatagtata ataaacgcca aaatccaatt aaagtttggg acctaggcgg 240
gcctcttacg aggctaactt atcgacaata agttaggtc 279

<210> 15
<211> 2237
<212> PRT
<213> grapevine leafroll-associated virus 3

<400> 15
Met Asp Tyr Ile Arg Pro Leu Arg Val Phe Ser Phe Pro His Val Asn
1 5 10 15

Asn Thr Leu Glu Tyr Val Arg Tyr Asn Lys Ala Asn Gly Asp Val Gly
20 25 30

Ala Phe Leu Thr Thr Met Lys Phe Ile Gly Asn Val Lys Leu Ser Asp
35 40 45

Phe Thr Pro Arg Cys Ala Ala Met Ile Tyr Ile Gly Lys Leu Thr Lys
50 55 60

Gly Val Lys Arg Thr Phe Val Pro Pro Pro Val Lys Gly Phe Ala Arg

65 70 75 80

Gln Tyr Ala Val Val Ser Gly Ser Val Ser Ala Leu Arg Gly Asp Gly
85 90 95

Lys Lys Val Leu Met Glu Ala Arg Thr Ser Thr Ser Ala Thr Ser Asp
100 105 110

Val Ser Asp Phe Asp Val Val Phe Glu Ala Val Ser Asn Ala Leu Leu
115 120 125

Val Val His Tyr His Arg Val Val Pro Tyr Ala Pro Val Lys Arg Glu
130 135 140

Gln Pro Lys Pro Ala Val Lys Gln Asp Glu Gln Lys Pro Lys Arg Gln
145 150 155 160

Ala Ser His Trp Ala Val Lys Pro Thr Ala Val Gly Val His Val Pro
165 170 175

Leu Pro Lys Lys Gln Glu Ala Leu Glu Pro Ala Gln Ser Val Pro Gln
180 185 190

Gln Ser Leu Glu Glu Lys Ala Ala Leu Thr Phe Gly Leu Phe Phe Ser
195 200 205

Lys Gly Gly Gly Asp Glu Ser Asp Ala Val Ile Leu Arg Lys Gly Lys
210 215 220

Leu Phe Asn Arg Ala Leu Asn Val Pro Ile Asp Val Lys Asn Thr Phe
225 230 235 240

Val Trp Ala Lys Ile Trp Asp Glu Ala Ser Arg Arg Arg Gly Tyr Phe
245 250 255

Tyr Val Lys Asp Arg Ala Val Lys Phe Phe Pro Ile Val Arg Gly Arg
260 265 270

Ala Thr Ile Glu Asp Phe Ile Val Asn Thr Ala Pro Gly Cys Asp Val
275 280 285

Ala Leu Pro Arg Ile Glu Leu Trp Ser Met Arg Glu Arg Ala Phe Val
290 295 300

Cys Thr Thr Lys Gly Trp Cys Trp Phe Asn Asn Glu Arg Leu Arg Gly
305 310 315 320

Glu Ile Tyr Arg Arg Arg Cys Phe Ser Ser Ser Phe Ser Ile Gly Phe

325 330 335

Leu Met His Leu Gly Phe Arg Ser Leu Lys Val Ile Arg Phe Ala Gly
340 345 350

Thr Asn Ile Leu His Met Pro Ser Leu Asn Glu Glu Arg Thr Phe Gly
355 360 365

Trp Lys Gly Gly Asp Val Tyr Leu Pro Asn Val Pro Lys Thr Ala Ile
370 375 380

Val Ala Gly Asp Arg Thr Arg Leu Gly Gly Glu Ile Leu Ala Ser Val
385 390 395 400

Ala Asn Ala Leu Asn Gln Glu Glu Val Tyr Ser Ser Val Val Ser Ser
405 410 415

Ile Thr Asn Arg Leu Val Leu Arg Asp Gln Ser Ala Leu Leu Ser His
420 425 430

Leu Asp Thr Lys Leu Cys Asp Met Phe Ser Gln Arg Asp Ala Met Ile
435 440 445

Arg Glu Lys Pro Ser His Arg Cys Asp Val Phe Leu Lys Pro Arg Glu
450 455 460

Arg Glu Lys Leu Arg Glu Leu Phe Pro Glu Leu Ser Ile Gln Phe Ser
465 470 475 480

Asp Ser Val Arg Ser Ser His Pro Phe Ala Asn Ala Met Arg Ser Cys
485 490 495

Phe Asn Gly Ile Phe Ser Arg Arg Cys Gly Asn Val Cys Phe Phe Asp
500 505 510

Ile Gly Gly Ser Phe Thr Tyr His Val Lys Ala Gly His Val Asn Cys
515 520 525

His Val Cys Asn Pro Val Leu Asp Val Lys Asp Val Lys Arg Arg Ile
530 535 540

Asn Glu Ile Leu Phe Leu Ser Thr Ala Gly Gly Asp Ser Tyr Val Ser
545 550 555 560

Ser Asp Leu Leu Thr Glu Ala Ala Ser Lys Ser Val Ser Tyr Cys Ser
565 570 575

Arg Glu Ser Gln Asn Cys Asp Ser Arg Ala Asp Ala Gly Phe Met Val

580 585 590

Asp Val Tyr Asp Ile Ser Pro Gln Gln Val Ala Glu Ala Met Asp Lys
595 600 605

Lys Gly Ala Leu Val Phe Asp Ile Ala Leu Met Phe Pro Val Glu Leu
610 615 620

Leu Tyr Gly Asn Gly Glu Val Tyr Leu Glu Glu Leu Asp Thr Leu Val
625 630 635 640

Lys Arg Glu Gly Asp Tyr Leu Ala Tyr Asn Val Gly Gln Cys Gly Glu
645 650 655

Met Tyr Glu His Ser Phe Ser Asn Val Ser Gly Phe Phe Thr Phe Ser
660 665 670

Tyr Val Arg Thr Ser Ser Gly Asn Val Phe Lys Leu Glu Tyr Glu Gly
675 680 685

Tyr Arg Cys Gly Tyr His His Leu Thr Met Cys Arg Ala Gln Lys Ser
690 695 700

Pro Gly Thr Glu Val Thr Tyr Arg Ser Leu Val Pro Ser Phe Val Gly
705 710 715 720

Lys Ser Leu Val Phe Ile Pro Val Val Ala Gly Ser Ser Val Ser Phe
725 730 735

Lys Thr Ile Val Leu Asp Ser Asp Phe Val Asp Arg Ile Tyr Ser Tyr
740 745 750

Ala Leu Asn Thr Ile Gly Thr Phe Glu Asn Arg Thr Phe Glu Tyr Ala
755 760 765

Val Gly Ala Val Arg Ser Gln Lys Thr His Val Ile Thr Gly Ser Arg
770 775 780

Val Val His Ser Lys Val Asp Ile Ser Pro Asp Asp Met Trp Gly Leu
785 790 795 800

Val Val Ala Val Met Ala Gln Ala Ile Lys Asp Arg Ala Lys Ser Ile
805 810 815

Arg Ser Tyr Asn Phe Ile Lys Ala Ser Glu Gly Ser Leu Ala Gly Val
820 825 830

Phe Lys Leu Phe Phe Gln Thr Val Gly Asp Cys Phe Ser Asn Ala Val

835 840 845

Ser Val Tyr Ala Lys Ala Met Val His Asp Asn Phe Asn Val Leu Glu
850 855 860

Thr Leu Met Ser Met Pro Arg Ala Phe Ile Arg Lys Val Pro Gly Ser
865 870 875 880

Val Val Val Thr Ile Cys Thr Ser Gly Ala Ser Asp Arg Leu Glu Leu
885 890 895

Arg Gly Ala Phe Asp Ile Ser Lys Glu Thr Phe Gly Arg Lys Leu Lys
900 905 910

Asn Ser Arg Leu Arg Val Phe Ser Arg Ala Ile Val Glu Asp Ser Ile
915 920 925

Lys Val Met Lys Ala Met Lys Thr Glu Asp Gly Lys Pro Leu Pro Ile
930 935 940

Thr Glu Asp Ser Val Tyr Ala Phe Ile Met Gly Asn Val Ser Asn Val
945 950 955 960

His Cys Thr Arg Ala Gly Leu Leu Gly Gly Ser Lys Ala Thr Val Val
965 970 975

Ser Ser Val Ser Lys Gly Leu Val Ala Arg Gly Ala Ala Thr Lys Ala
980 985 990

Phe Ser Gly Ile Thr Ser Phe Phe Ser Thr Gly Ser Leu Phe Tyr Asp
995 1000 1005

Arg Gly Leu Thr Glu Asp Glu Arg Leu Asp Ala Leu Val Arg Thr Glu
1010 1015 1020

Asn Ala Ile Asn Ser Pro Val Gly Ile Leu Glu Thr Ser Arg Val Ala
1025 1030 1035 1040

Val Ser Lys Val Val Ala Gly Thr Lys Glu Phe Trp Ser Glu Val Ser
1045 1050 1055

Leu Asn Asp Phe Thr Thr Phe Val Leu Arg Asn Lys Val Leu Ile Gly
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Ile Phe Val Ala Ser Leu Gly Ala Ala Pro Ile Ala Trp Lys Tyr Arg
1075 1080 1085

Arg Gly Ile Ala Ala Asn Ala Arg Arg Tyr Ala Gly Ser Ser Tyr Glu

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    1090                1095                1100

Thr Leu Ser Ser Leu Ser Ser Gln Ala Ala Gly Gly Leu Arg Gly Leu
1105                1110                1115                1120

Thr Ser Ser Thr Val Ser Gly Gly Ser Leu Val Val Arg Arg Gly Phe
                1125                1130                1135

Ser Ser Ala Val Thr Val Thr Arg Ala Thr Val Ala Lys Arg Gln Val
            1140                1145                1150

Pro Leu Ala Leu Leu Ser Phe Ser Thr Ser Tyr Ala Ile Ser Gly Cys
        1155                1160                1165

Ser Met Leu Gly Ile Trp Ala His Ala Leu Pro Arg His Leu Met Phe
    1170                1175                1180

Phe Phe Gly Leu Gly Thr Leu Leu Gly Ala Arg Ala Ser Ala Asn Thr
1185                1190                1195                1200

Trp Lys Phe Gly Gly Phe Ser Asn Asn Trp Cys Ala Val Pro Glu Val
                1205                1210                1215

Val Trp Arg Gly Lys Ser Val Ser Ser Leu Leu Leu Pro Ile Thr Leu
            1220                1225                1230

Gly Val Ser Leu Ile Ile Arg Gly Leu Leu Asn Asp Thr Ile Pro Gln
        1235                1240                1245

Leu Ala Tyr Val Pro Pro Val Glu Gly Arg Asn Val Tyr Asp Glu Thr
    1250                1255                1260

Leu Arg Tyr Tyr Arg Asp Phe Asp Tyr Asp Glu Gly Ala Gly Pro Ser
1265                1270                1275                1280

Gly Thr Gln His Glu Ala Val Pro Gly Asp Asp Asn Asp Gly Ser Thr
                1285                1290                1295

Ser Ser Val Ser Ser Tyr Asp Val Val Thr Asn Val Arg Asp Val Gly
            1300                1305                1310

Ile Ser Thr Asn Gly Glu Val Thr Gly Glu Glu Glu Thr His Ser Pro
        1315                1320                1325

Arg Ser Val Gln Tyr Thr Tyr Val Glu Glu Glu Val Ala Pro Ser Ala
    1330                1335                1340

Ala Val Ala Glu Arg Gln Gly Asp Pro Ser Gly Ser Gly Thr Ala Asp
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1345 1350 1355 1360

Ala Met Ala Phe Val Glu Ser Val Lys Lys Gly Val Asp Asp Val Phe
1365 1370 1375

His Gln Gln Ser Ser Gly Glu Thr Ala Arg Glu Val Glu Val Asp Gly
1380 1385 1390

Lys Gly Leu Leu Pro Glu Ser Val Val Gly Glu Ala Pro Thr Gln Glu
1395 1400 1405

Arg Gly Arg Ala Ala Asp Gly Asn Thr Ala Gln Thr Ala Val Asn Glu
1410 1415 1420

Gly Asp Arg Glu Pro Val Gln Ser Ser Leu Val Ser Ser Pro Gln Ala
1425 1430 1435 1440

Asp Ile Pro Lys Val Thr Gln Ser Glu Val His Ala Gln Lys Glu Val
1445 1450 1455

Lys Gln Glu Val Pro Leu Ala Thr Val Ser Gly Ala Thr Pro Ile Val
1460 1465 1470

Asp Glu Lys Pro Ala Pro Ser Val Thr Thr Arg Gly Val Lys Ile Ile
1475 1480 1485

Asp Lys Gly Lys Ala Val Ala His Val Ala Glu Lys Lys Gln Val Gln
1490 1495 1500

Val Glu Gln Pro Lys Gln Arg Ser Leu Thr Ile Asn Glu Gly Lys Ala
1505 1510 1515 1520

Gly Lys Gln Leu Cys Met Phe Arg Thr Cys Ser Cys Gly Val Gln Leu
1525 1530 1535

Asp Val Tyr Asn Glu Ala Thr Ile Ala Thr Arg Phe Ser Asn Ala Phe
1540 1545 1550

Thr Phe Val Asp Asn Leu Lys Gly Arg Ser Ala Val Phe Phe Ser Lys
1555 1560 1565

Leu Gly Glu Gly Tyr Thr Tyr Asn Gly Gly Ser His Val Ser Ser Gly
1570 1575 1580

Trp Pro Arg Ala Leu Glu Asp Ile Leu Thr Ala Ile Lys Tyr Pro Ser
1585 1590 1595 1600

Val Phe Asp His Cys Leu Val Gln Lys Tyr Lys Met Gly Gly Gly Val

1605 1610 1615

Pro Phe His Ala Asp Asp Glu Glu Cys Tyr Pro Ser Asp Asn Pro Ile
1620 1625 1630

Leu Thr Val Asn Leu Val Gly Lys Ala Asn Phe Ser Thr Lys Cys Arg
1635 1640 1645

Lys Gly Gly Lys Val Met Val Ile Asn Val Ala Ser Gly Asp Tyr Phe
1650 1655 1660

Leu Met Pro Cys Gly Phe Gln Arg Thr His Leu His Ser Val Asn Ser
1665 1670 1675 1680

Ile Asp Glu Gly Arg Ile Ser Leu Thr Phe Arg Ala Thr Arg Arg Val
1685 1690 1695

Phe Gly Val Gly Arg Met Leu Gln Leu Ala Gly Gly Val Ser Asp Glu
1700 1705 1710

Lys Ser Pro Gly Val Pro Asn Gln Gln Pro Gln Ser Gln Gly Ala Thr
1715 1720 1725

Arg Thr Ile Thr Pro Lys Ser Gly Gly Lys Ala Leu Ser Glu Gly Ser
1730 1735 1740

Gly Arg Glu Val Lys Gly Arg Ser Thr Tyr Ser Ile Trp Cys Glu Gln
1745 1750 1755 1760

Asp Tyr Val Arg Lys Cys Glu Trp Leu Arg Ala Asp Asn Pro Val Met
1765 1770 1775

Ala Leu Glu Pro Asp Tyr Thr Pro Met Thr Phe Glu Val Val Lys Thr
1780 1785 1790

Gly Thr Ser Glu Asp Ala Val Val Glu Tyr Leu Lys Tyr Leu Ala Ile
1795 1800 1805

Gly Ile Glu Arg Thr Tyr Arg Ala Leu Leu Met Ala Arg Asn Ile Ala
1810 1815 1820

Val Thr Thr Ala Glu Gly Val Leu Lys Val Pro Asn Gln Val Tyr Glu
1825 1830 1835 1840

Ser Leu Pro Gly Phe His Val Tyr Lys Ser Gly Thr Asp Leu Ile Phe
1845 1850 1855

His Ser Thr Gln Asp Gly Leu Arg Val Arg Asp Leu Pro Tyr Val Leu

1860 1865 1870

Ile Ala Glu Lys Gly Ile Phe Thr Lys Gly Lys Asp Val Asp Ala Val
1875 1880 1885

Val Ala Leu Gly Asp Asn Leu Phe Val Cys Asp Asp Ile Leu Val Phe
1890 1895 1900

His Asp Ala Ile Asn Leu Ile Gly Ala Leu Lys Val Ala Arg Cys Gly
1905 1910 1915 1920

Met Val Gly Glu Ser Phe Lys Ser Phe Glu Tyr Lys Cys Tyr Asn Ala
1925 1930 1935

Pro Pro Gly Gly Gly Lys Thr Thr Thr Leu Val Asp Glu Phe Val Lys
1940 1945 1950

Ser Pro Asn Ser Thr Ala Thr Ile Thr Ala Asn Val Gly Ser Ser Glu
1955 1960 1965

Asp Ile Asn Met Ala Val Lys Lys Arg Asp Pro Asn Leu Glu Gly Leu
1970 1975 1980

Asn Ser Ala Thr Thr Val Asn Ser Arg Val Val Asn Phe Ile Val Arg
1985 1990 1995 2000

Gly Met Tyr Lys Arg Val Leu Val Asp Glu Val His Met Met His Gln
2005 2010 2015

Gly Leu Leu Gln Leu Gly Val Phe Ala Thr Gly Ala Ser Glu Gly Leu
2020 2025 2030

Phe Phe Gly Asp Ile Asn Gln Ile Pro Phe Ile Asn Arg Glu Lys Val
2035 2040 2045

Phe Arg Met Asp Cys Ala Val Phe Val Pro Lys Lys Glu Ser Val Val
2050 2055 2060

Tyr Thr Ser Lys Ser Tyr Arg Cys Pro Leu Asp Val Cys Tyr Leu Leu
2065 2070 2075 2080

Ser Ser Met Thr Val Arg Gly Thr Glu Lys Cys Tyr Pro Glu Lys Val
2085 2090 2095

Val Ser Gly Lys Asp Lys Pro Val Val Arg Ser Leu Ser Lys Arg Pro
2100 2105 2110

Ile Gly Thr Thr Asp Asp Val Ala Glu Ile Asn Ala Asp Val Tyr Leu

2115 2120 2125

Cys Met Thr Gln Leu Glu Lys Ser Asp Met Lys Arg Ser Leu Lys Gly
2130 2135 2140

Lys Gly Lys Glu Thr Pro Val Met Thr Val His Glu Ala Gln Gly Lys
2145 2150 2155 2160

Thr Phe Ser Asp Val Val Leu Phe Arg Thr Lys Lys Ala Asp Asp Ser
2165 2170 2175

Leu Phe Thr Lys Gln Pro His Ile Leu Val Gly Leu Ser Arg His Thr
2180 2185 2190

Arg Ser Leu Val Tyr Ala Ala Leu Ser Ser Lys Leu Asp Asp Lys Val
2195 2200 2205

Gly Thr Tyr Ile Ser Asp Ala Ser Pro Gln Ser Val Ser Asp Ala Leu
2210 2215 2220

Leu His Thr Phe Ala Pro Ala Gly Cys Phe Arg Gly Ile
2225 2230 2235

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/09307

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/54 C12N15/55 C12N15/61 C12N15/82 C12N9/90
C12N9/50 C12N9/10 C12N5/10 C12Q1/68 C07K16/08
A01H5/00 G01N33/563

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K C12N C12Q G01N A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 22700 A (CORNELL RES FOUNDATION INC) 26 June 1997 (1997-06-26) cited in the application the whole document; esp. example 13; claims	1-34
A	FAZELI C.: "AC U22158" EMBL DATABASE,28 June 1995 (1995-06-28), XP002113446 Heidelberg the whole document	7

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 August 1999	10/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kania, T

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MINAFRA A. AND HADIDI A.: "Sensitive detection of grapevine virus A, B, or leafroll-associated III from viruliferous mealybugs and infected tissue by cDNA amplification" JOURNAL OF VIROLOGICAL METHODS, vol. 47, 1994, pages 175-188, XP000675981 cited in the application the whole document	32-34
A	EP 0 769 696 A (AGRITOPE INC) 23 April 1997 (1997-04-23) the whole document	32-34
A	DOLJA V. ET AL.: "Molecular biology and evolution of closteroviruses: Sophisticated build-up of large RNA genomes" ANNUAL REVIEWS ON PHYTOPATHOLOGY, vol. 32, 1994, pages 261-285, XP000675908 cited in the application the whole document	1-34
P,X	LING, K. -S. ET AL: "Nucleotide sequence of the 3'-terminal two-thirds of the grapevine-- leafroll - associated virus - 3 genome reveals a typical monopartite closterovirus" J. GEN. VIROL. (1998), 79(5), 1299-1307, XP002113447 the whole document	1-34

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/09307

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/09307

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9722700 A	26-06-1997	AU 1688997 A	14-07-1997
		CA 2242402 A	26-06-1997
		EP 0896624 A	17-02-1999
		NZ 330834 A	29-06-1999
EP 0769696 A	23-04-1997	NONE	